REMARKS

Claims 1, 4, 8-30, and 77-79 are pending are pending. New claims 78-79 have been added. Support for the new claims can be found at, *e.g.*, page 28, line 10 to page 30, line 27. No new matter has been added.

Claim Rejection under 35 U.S.C. §103 (a)

Claims 1, 4, 8-40 and 77 were rejected under 35 U.S.C. §103 (a) as obvious over Paul in view of Fukushima, Bova, and Mandeville. Applicants traverse.

The claimed invention relates to a method for decreasing serum cholesterol and increasing serum HDL in a patient by administering a composition including *Bacillus coagulans* bacteria.

The Examiner admits that Paul does not teach a method using a *Bacillus* species, much less the specific *Bacillus coagulans* strain as required by the pending claims. (Office action at page 6). However, the Examiner asserts that it would have been obvious to one of ordinary skill in the art to use a *Bacillus,* because Fukushima teaches the effect of a probiotic containing *Bacillus* to reduce serum cholesterol and increase serum HDL. (Id.). The Examiner also states that:

> [a]lthough the references do not specifically name a Bacillus coagulans, one of ordinary skill in the art would certainly have been motivated by the cited references to use any known lactic acid bacteria in the composition and methods of Paul with a reasonable expectation for successfully decreasing serum cholesterol and increasing serum HDL. Absence of evidence regarding any unexpected advantage or benefit using the claimed bacteria, the claims remain obvious for these reasons and those made above.
> (Office action at page 9).

First, Applicants believe that the Examiner's reliance on Fukushima is misplaced. Fukushima does not describe or suggest *Bacillus coagulans* bacteria, the strain to which the pending claims are drawn. The species of Bacillus, *Bacillus coagulans* is simply not present in any of the cited references. Given the diversity of the species within the *Bacillus* genus, there is no rationale for choosing *Bacillus coagulans* based on a description of using another species of *Bacillus*. It is known to those skilled in the art that *Bacillus coagulans* is one species of hundreds of *Bacillus* species contained within either the forty recognized species in the genus *Bacillus*

(listed in Bergey's Manual of Systematic Bacteriology Vol 2 (1986)) or the over 200 *Bacillus* species identified as *species incertae sedis* (species of uncertain standing).

Fukushima provides a probiotic composition containing twelve different microorganisms - a combination of three different species of *Bacillus* (*Bacillus subtilis*, *Bacillus natto*, and *Bacillus megaterium*), four different species of *Lactobacillus* (*Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus brevis*, and *Lactobacillus casei*), three different species of *Streptococcus* (*Streptococcus faecalis*, *Streptococcus lactis*, and *Streptococcus thermophilus*), and two different species of yeast (*Saccharomyces cerevisiae* and *Candida utilis*), all in amounts that vary ten-fold between components. (See Fukushima, Table 1 on page 703). Fukushima provides no information as to what microorganisms in the mixture is/are responsible for the cholesterol-reducing property of the mixture. In the absence of such information, one of skilled in the art would interpret the teachings of Fukushima to mean that the mixture (*i.e.*, all of the microorganisms listed) is required to achieve cholesterol reduction. The reference fails to point to Bacillus as the cholesterol-reducing component of the mixture. Even if it did, the teachings of Fukushima fails to suggest to one skilled in the art to "use any known lactic acid bacteria," as suggested by the Examiner, since there is no unifying theme or common characteristic among the three *Bacillus* species listed.

The distinguishing feature of members of the *Bacillus* genus is the production of endospores. Bacillus is distinguished from other endospore-producing bacteria by the following characteristics: strict or facultative aerobe, rod-shaped, and (usually) catalase-positive. Beyond that, the family includes a wide ranges of species from the deadly *Bacillus anthracis* to pathogenic *Bacillus cereus,* which is responsible for severe gastrointestinal distress, to heat and acid-tolerant *Bacillus stearothermophilus* to insect pathogen *Bacillus thuringiensis.* One skilled in the art would not conclude that if the *Bacillus* species used by Fukushima were effective in lowering serum cholesterol, that any other *Bacillus* species would be equally effective. Thus, the Examiner has not presented the required *prima facie* demonstration that one would be motivated to combine the *Bacillus* strain(s) disclosed by Fukushima in the methods and compositions of Paul, much less the specific *Bacillus coagulans* strain required by the pending claims.

Second, Applicants submit that the claimed compositions have an unexpected advantage or benefit. "A greater than expected result is an evidentiary factor pertinent to the legal

conclusion of obviousness ... of the claims at issue." In re Corkill, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). *See*, also, MPEP 716.02(a). The accompanying Declaration of Sean Farmer ("Farmer Declaration") states that the administration of the *Bacillus coagulans*-containing probiotic composition reduced total serum cholesterol over 20% in human subjects over the course of the clinical trial. Farmer Declaration at ¶ 6. Fukushima teaches that mixture described in Table 1, containing twelve different microorganisms, results in a decrease in total serum cholesterol of 16.0% in rats fed a high-fat, high-cholesterol diet, and 4.4% in rats fed a basal diet. (See Fukushima, Table 3 on page 705). There is no teaching in Fukushima that suggests that any one organism of the twelve listed is responsible for cholesterol reduction. Even if the reference did point to the *Bacillus* genus, the combination of references falls short of suggesting the claimed species, *Bacillus coagulans*, and falls short of suggesting its use to reduce cholesterol in humans. The data presented by Mr. Farmer indicates that the claimed compositions produce a surprising reduction of cholesterol in humans. Fukushima does not teach or suggest that the disclosed probiotic composition would have a similar effect in decreasing total serum cholesterol in humans. Therefore, there is no motivation for one of ordinary skill in the art to combine a single component of the complex mixture disclosed by Fukushima in the methods and compositions of Paul with any reasonable expectation of success. Therefore, the pending claims are not obvious, and this rejection should be withdrawn.

The remaining references, Bova and Mandeville, do not remedy the deficiency of Paul and Fukushima, since neither Bova nor Mandeville link *Bacillus coagulans* with serum cholesterol. Applicants therefore request that this rejection be withdrawn.

CONCLUSION

Based on the instant amendments and remarks, Applicants submit that this application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact Applicants' undersigned attorney at the telephone number indicated below.

Respectfully submitted,

Reg No 48223

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